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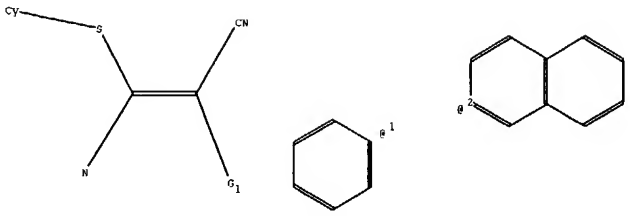

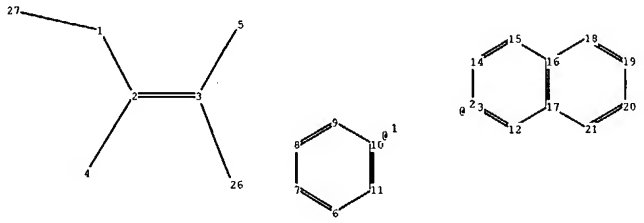

chain nodes :
1 2 3 4 5 26 27
ring nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
1-2 1-27 2-3 2-4 3-5 3-26
ring bonds :
6-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14 14-15 15-16 16-17 16-18 17-21
18-19 19-20 20-21
exact/norm bonds :
1-2 1-27 2-4 3-26
exact bonds :
2-3 3-5
normalized bonds :
6-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14 14-15 15-16 16-17 16-18 17-21
18-19 19-20 20-21
isolated ring systems :
containing 6 : 12 :

G1:[*1],[*2]

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 26:CLASS 27:Atom

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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1            Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2            "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27    Source of Registration (SR) information in REGISTRY updated
                    and searchable
 NEWS  4  JAN 27    A new search aid, the Company Name Thesaurus, available in
                    CA/CAplus
 NEWS  5  FEB 05    German (DE) application and patent publication number format
                    changes
 NEWS  6  MAR 03    MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03    MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03    FRANCEPAT now available on STN
 NEWS  9  MAR 29    Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29    WPIFV now available on STN
 NEWS 11  MAR 29    New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 12  APR 26    PROMT: New display field available
 NEWS 13  APR 26    IFIPAT/IFIUDB/IFICDB: New super search and display field
                    available
 NEWS 14  APR 26    LITALERT now available on STN
 NEWS 15  APR 27    NLDB: New search and display fields available
 NEWS 16  May 10    PROUSDDR now available on STN
 NEWS 17  May 19    PROUSDDR: One FREE connect hour, per account, in both May
                    and June 2004
 NEWS 18  May 12    EXTEND option available in structure searching
 NEWS 19  May 12    Polymer links for the POLYLINK command completed in REGISTRY
 NEWS 20  May 17    FRFULL now available on STN
 NEWS 21  May 27    STN User Update to be held June 7 and June 8 at the SLA 2004
                    Conference
 NEWS 22  May 27    New UPM (Update Code Maximum) field for more efficient patent
                    SDIs in CAplus
 NEWS 23  May 27    CAplus super roles and document types searchable in REGISTRY
 NEWS 24  May 27    Explore APOLLIT with free connect time in June 2004

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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FILE 'HOME' ENTERED AT 07:20:50 ON 07 JUN 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21
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FILE 'REGISTRY' ENTERED AT 07:20:56 ON 07 JUN 2004
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STRUCTURE FILE UPDATES:    6 JUN 2004  HIGHEST RN 690209-28-0
DICTIONARY FILE UPDATES:   6 JUN 2004  HIGHEST RN 690209-28-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L1      STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1              STR

=> s l1
SAMPLE SEARCH INITIATED 07:22:44 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     14 TO ITERATE

100.0% PROCESSED      14 ITERATIONS                              4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO      504
PROJECTED ANSWERS:               4 TO      200

L2            4 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 07:22:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    293 TO ITERATE

100.0% PROCESSED     293 ITERATIONS                             84 ANSWERS
SEARCH TIME: 00.00.01

L3           84 SEA SSS FUL L1

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY     SESSION
FULL ESTIMATED COST                             156.26      156.47
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FILE 'HCAPLUS' ENTERED AT 07:22:51 ON 07 JUN 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 7 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 6 Jun 2004 (20040606/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L4          12 L3

=> s l4 and hobbs, f?/au
            61 HOBBS, F?/AU
L5           1 L4 AND HOBBS, F?/AU

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L4   ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

ACCESSION NUMBER: 2003:661438 HCAPLUS
DOCUMENT NUMBER: 140:87531
TITLE: The role of the extracellular signal-regulated kinase signaling pathway in mood modulation
AUTHOR(S): Einat, Haim; Yuan, Peixiong; Gould, Todd D.; Li, Jianling; Du, JianHua; Zhang, Lei; Manji, Husseini K.; Chen, Guang
CORPORATE SOURCE: Laboratory of Molecular Pathophysiology, Mood and Anxiety Disorders Program, National Institute of Mental Health, Department of Health and Human Services, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Neuroscience (2003), 23(19), 7311-7316
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

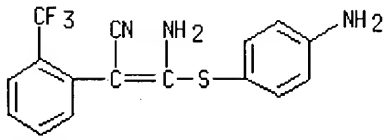
AB The neurobiol. underpinnings of mood modulation, mol. pathophysiol. of manic-depressive illness, and therapeutic mechanism of mood stabilizers are largely unknown. The extracellular signal-regulated kinase (ERK) pathway is activated by neurotrophins and other neuroactive chems. to produce their effects on neuronal differentiation, survival, regeneration, and structural and functional plasticity. We found that lithium and valproate, commonly used mood stabilizers for the treatment of

manic-depressive illness, stimulated the ERK pathway in the rat hippocampus and frontal cortex. Both drugs increased the levels of activated phospho-ERK44/42, activated phospho-ribosomal protein S6 kinase-1 (RSK1) (a substrate of ERK), phospho-CREB (cAMP response element-binding protein) and phospho-B cell lymphoma protein-2 antagonist of cell death (substrates of RSK), and BDNF. Inhibiting the ERK pathway with the blood-brain barrier-penetrating mitogen-activated protein kinase (MAP kinase)/ERK kinase (MEK) kinase inhibitor SL327, but not with the nonblood-brain barrier-penetrating MEK inhibitor U0126, decreased immobility time and increased swimming time of rats in the forced-swim test. SL327, but not U0126, also increased locomotion time and distance traveled in a large open field. The behavioral changes in the open field were prevented with chronic lithium pretreatment. SL327-induced behavioral changes are qual. similar to the changes induced by amphetamine, a compd. that induces relapse in remitted manic patients and mood elevation in normal subjects. These data suggest that the ERK pathway may mediate the antimanic effects of mood stabilizers.

IT 305350-87-2, SL 327
RL: PAC (Pharmacological activity); BIOL (Biological study)
(role of the extracellular signal-regulated kinase signaling pathway in mood modulation)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     (FILE 'HOME' ENTERED AT 07:20:50 ON 07 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 07:20:56 ON 07 JUN 2004
L1               STRUCTURE UPLOADED
L2             4 S L1
L3            84 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 07:22:51 ON 07 JUN 2004
L4            12 S L3
L5             1 S L4 AND HOBBS, F?/AU

=> s l4 not l5
L6            11 L4 NOT L5

=> d l6, ibib abs fhitstr, 1-11

L6   ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:          2003:661438  HCAPLUS
DOCUMENT NUMBER:           140:87531
TITLE:                     The role of the extracellular signal-regulated kinase
                           signaling pathway in mood modulation
```

AUTHOR(S): Einat, Haim; Yuan, Peixiong; Gould, Todd D.; Li, Jianling; Du, JianHua; Zhang, Lei; Manji, Husseini K.; Chen, Guang

CORPORATE SOURCE: Laboratory of Molecular Pathophysiology, Mood and Anxiety Disorders Program, National Institute of Mental Health, Department of Health and Human Services, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Journal of Neuroscience (2003), 23(19), 7311-7316
CODEN: JNRSDS; ISSN: 0270-6474

PUBLISHER: Society for Neuroscience

DOCUMENT TYPE: Journal

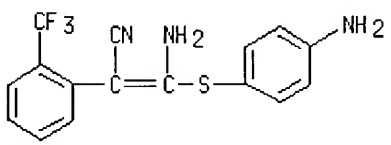
LANGUAGE: English

AB The neurobiol. underpinnings of mood modulation, mol. pathophysiol. of manic-depressive illness, and therapeutic mechanism of mood stabilizers are largely unknown. The extracellular signal-regulated kinase (ERK) pathway is activated by neurotrophins and other neuroactive chems. to produce their effects on neuronal differentiation, survival, regeneration, and structural and functional plasticity. We found that lithium and valproate, commonly used mood stabilizers for the treatment of manic-depressive illness, stimulated the ERK pathway in the rat hippocampus and frontal cortex. Both drugs increased the levels of activated phospho-ERK44/42, activated phospho-ribosomal protein S6 kinase-1 (RSK1) (a substrate of ERK), phospho-CREB (cAMP response element-binding protein) and phospho-B cell lymphoma protein-2 antagonist of cell death (substrates of RSK), and BDNF. Inhibiting the ERK pathway with the blood-brain barrier-penetrating mitogen-activated protein kinase (MAP kinase)/ERK kinase (MEK) kinase inhibitor SL327, but not with the nonblood-brain barrier-penetrating MEK inhibitor U0126, decreased immobility time and increased swimming time of rats in the forced-swim test. SL327, but not U0126, also increased locomotion time and distance traveled in a large open field. The behavioral changes in the open field were prevented with chronic lithium pretreatment. SL327-induced behavioral changes are qual. similar to the changes induced by amphetamine, a compd. that induces relapse in remitted manic patients and mood elevation in normal subjects. These data suggest that the ERK pathway may mediate the antimanic effects of mood stabilizers.

IT **305350-87-2**, SL 327
RL: PAC (Pharmacological activity); BIOL (Biological study)
(role of the extracellular signal-regulated kinase signaling pathway in mood modulation)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:153388 HCAPLUS

DOCUMENT NUMBER: 138:198569

TITLE: Use of kinase-inhibiting agents for prophylaxis and/or

therapy of viral diseases, and system for identification of such agents

INVENTOR(S): Ludwig, Stephan; Planz, Oliver; Sedlacek, Hans-Harald; Pleschka, Stephan

PATENT ASSIGNEE(S): Medinnova Gesellschaft fur Medizinische Innovationen aus Akademischer Forschung m.b.H., Germany

SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10138912	A1	20030227	DE 2001-10138912	20010808
WO 2003015689	A2	20030227	WO 2002-DE2810	20020726

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

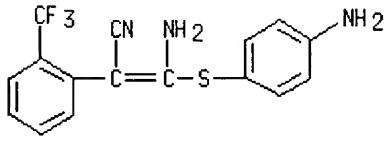
PRIORITY APPLN. INFO.: DE 2001-10138912 A 20010808

AB The invention discloses the use of at least one, preferably two, active substance(s) for the prophylaxis and/or therapy of at least one viral disease, characterized in that the active substance(s) inhibit either a signal transduction pathway-assocd. kinase such that virus replication is essentially inhibited or a SEK kinase.

IT 305350-87-2, SL 327
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kinase-inhibiting agents for prophylaxis and/or therapy of viral diseases, and system for identification of such agents)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:12017 HCAPLUS

DOCUMENT NUMBER: 138:396146

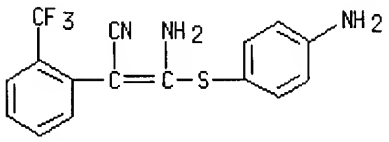
TITLE: Significant neuroprotection against ischemic brain injury by inhibition of the MEK1 protein kinase in mice: Exploration of potential mechanism associated with apoptosis

AUTHOR(S): Wang, Xinkang; Wang, Hugh; Xu, Lin; Rozanski, Dennis J.; Sugawara, Taku; Chan, Pak H.; Trzaskos, James M.; Feuerstein, Giora Z.
CORPORATE SOURCE: Department of Cardiovascular Sciences, Bristol-Myers Squibb Company, Wilmington, DE, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(1), 172-178
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB MEK1/2 is a serine/threonine protein kinase that phosphorylates and activates extracellular signal-responsive kinase (ERK)1/2. In the present study we explored the role of MEK1/2 in ischemic brain injury using a selective MEK1/2 inhibitor, SL327, in mice. C57BL/6 mice were subjected to a 30-min occlusion of the middle cerebral artery (MCAO) followed by reperfusion. Western blot anal. demonstrated the immediate activation of MEK/ERK after reperfusion (within the first 10 min) in the ischemic brain; this activation was dose dependently blocked by SL327 (10-100 mg/kg, i.p.). A single dose of SL327 (100 mg/kg) administered 15 min before or 25 min after the onset of ischemia resulted in 63.6% ($n = 18$, $p < 0.001$) and 50.7% ($n = 18$, $p < 0.01$) redn. in infarct size, resp., compared with vehicle-treated mice. Similarly, SL327 significantly reduced neurol. deficits 1 to 3 days after reperfusion ($n = 12$, $p < 0.01$). The salutary effect of SL327-induced neuroprotection was independent of mitochondrial cytochrome c release or caspase-8-mediated apoptosis; however, SL327 markedly suppressed the levels of active caspase-3 and DNA fragmentation (as a measure of apoptosis) after ischemia/reperfusion. Our data suggest that the inhibition of MEK1/2 results in neuroprotection from reperfusion injury and that this protection may be assocd. with the redn. in apoptosis.

IT 305350-87-2, SL 327
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis-assocd. mechanism of neuroprotection against ischemic brain damage by inhibition of MEK1 protein kinase)

RN 305350-87-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:574917 HCAPLUS
DOCUMENT NUMBER: 137:135102
TITLE: Inhibition of extracellular signal-regulated kinases (ERKs) reduces or prevents both tolerance to and dependence on opioid analgesics and sensitization after painful stimulation
INVENTOR(S): Gutstein, Howard B.

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058687	A2	20020801	WO 2002-US2128	20020125
WO 2002058687	A3	20031009		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1377279	A2	20040107	EP 2002-717370	20020125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

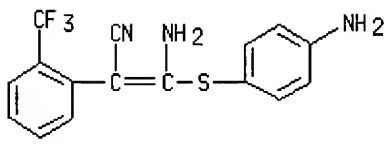
US 2001-264336P	P	20010125
WO 2002-US2128	W	20020125

AB Inhibition of mitogen-activated protein kinases (MAPKs), or more particularly extracellular signal-regulated kinases (ERKs) inhibits the development of tolerance to opioid analgesics. Therefore, methods for reducing tolerance, reducing the risk of phys. dependence, reducing hyperalgesia, reducing the symptoms of opioid withdrawal or inhibiting pain sensitization are described. MAPK inhibition at the spinal level represents a powerful treatment modality for chronic pain, blocking both neural sensitization induced by pain and factors limiting the effectiveness of opioids, the strongest analgesics currently in use to treat chronic pain.

IT **305350-87-2**, SL 327
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of extracellular signal-regulated kinases reduces or prevents tolerance to and dependence on opioid analgesics)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:256049 HCAPLUS
DOCUMENT NUMBER: 136:257237
TITLE: Tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of the "classical" mitogen activated protein (MAP) kinase pathway

INVENTOR(S): Dent, Paul; Grant, Steven; McKinstry, Robert; Dai, Yum
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026236	A1	20020404	WO 2001-US30508	20010928
WO 2002026236	C2	20030220		

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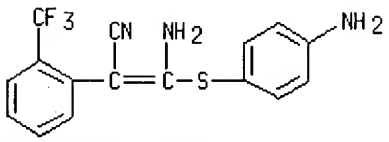
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-235938P P 20000928

AB The present invention provides a method for treating cancer by promoting apoptosis and reducing clonogenic survival of cancer cells. The method encompasses co-administering 1) a cell cycle checkpoint abrogation agent (for example, UCN-01 or caffeine) and 2) an inhibitor of a compensatory cytoprotective pathway, such as an agent that inhibits the MEK 1/2 pathway (e.g.; PD98059, U0126, or PD184352) or an agent that inhibits the PI 3 pathway (e.g.; LY294002 or wortmanin). In addn., because the co-administration step also radiosensitizes cancer cells, the method addnl. encompasses the administration of radiation to further reduce clonogenic survival of cancer cells. The method promotes apoptosis and reduces clonogenic survival in many types of cancer cells, including leukemia cells, prostate cancer cells, breast cancer cells, myeloma cells, and lymphoma cells.

IT **305350-87-2**, SL 327
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

RN 305350-87-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:31238 HCAPLUS
DOCUMENT NUMBER: 136:79789
TITLE: Methods for treating seizure disorders by inhibiting MAPK pathway activation

INVENTOR(S): Sweatt, J. David; Anderson, Anne E.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002097	A2	20020110	WO 2001-US20773	20010629
WO 2002002097	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002058699	A1	20020516	US 2001-893754	20010629

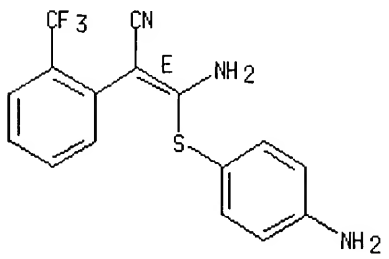
PRIORITY APPLN. INFO.: US 2000-215221P P 20000630
OTHER SOURCE(S): MARPAT 136:79789

AB Excessive brain neuronal excitability, assocd. with a seizure disorder, can be correlated with increased mitogen-activated protein kinase (MAPK) activity in neurons. Such excessive excitability can be ameliorated by administering an effective amt. of a compd., such as a MAPK phosphorylation or kinase activity inhibitor, that reduces the amt. of MAPK activity in neurons of an individual suffering from a seizure disorder. Compds. that inhibit phosphorylation or kinase activity of upstream activators or downstream targets of the MARPK cascade also are useful in this context.

IT **297744-40-2P**, (E)-SL 327
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anticonvulsant treatment with inhibitors of mitogen-activated protein kinase pathway activation)

RN 297744-40-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)-, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

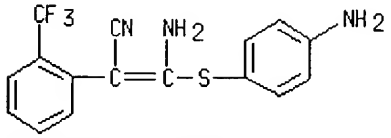
Full Text | Citing References

ACCESSION NUMBER: 2001:633052 HCAPLUS

DOCUMENT NUMBER: 136:63930
TITLE: Differential Regulation of IL-1β and TNF-α RNA Expression by MEK1 Inhibitor after Focal Cerebral Ischemia in Mice
AUTHOR(S): Wang, Hugh; Xu, Lin; Venkatachalam, Sivakami; Trzaskos, James M.; Friedman, Steven M.; Feuerstein, Giora Z.; Wang, Xinkang
CORPORATE SOURCE: Department of Cardiovascular Sciences, DuPont Pharmaceuticals Company, Experimental Station, Wilmington, DE, 19880, USA
SOURCE: Biochemical and Biophysical Research Communications (2001), 286(5), 869-874
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of the extracellular-signal-responsive kinase (ERK 1/2) by MAP kinase/ERK kinase (MEK1/2) following ischemia/reperfusion in the brain has been assocd. with cell death since inhibition of MEK1/2 provides neuroprotection in cerebral ischemia injury. Since inflammation has been implicated in ischemic brain injury, the present study investigated whether MEK1/2 modifies expression of two key inflammatory cytokines, IL-1β and TNFα, that have been shown to exacerbate ischemic brain injury. A mouse model of transient cerebral ischemia was deployed to test the effect of selective MEK1/2 inhibitor (SL327) on infarct size and cytokine expression. SL327 (100 mg/kg, i.p.) administered 15 min prior to ischemia resulted in 64% redn. in infarct size over controls (n = 8, P < 0.01). Under the same condition, SL327 significantly reduced peak expression of IL-1β mRNA (59% redn. compared to vehicle, P < 0.01, n = 4) but not TNF-α mRNA. A parallel redn. in IL-1β protein (67%, P < 0.05, n = 6) was also obsd. using ELISA anal. These data suggest that the neuroprotective effect of MEK1/2 inhibition may be mediated by suppression of IL-1β. The study also demonstrates for the first time that these two cytokines are differentially regulated by kinase mediated signaling pathways. (c) 2001 Academic Press.

IT 305350-87-2, SL327
RL: PAC (Pharmacological activity); BIOL (Biological study)
(differential regulation of IL-1β and TNF-α RNA expression by MEK1 inhibitor after focal cerebral ischemia in mice)
RN 305350-87-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2000:805039 HCAPLUS
DOCUMENT NUMBER: 133:344610
TITLE: Specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells

INVENTOR(S): Dent, Paul; Grant, Steven; Jarvis, W. David
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6147107	A	20001114	US 1998-203342	19981220

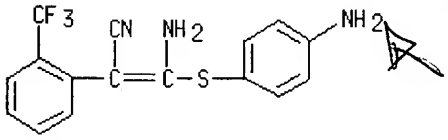
PRIORITY APPLN. INFO.: US 1998-203342 19981220

AB Mammalian cancer cells are effectively killed when treated with a lethal agent (e.g. radiation or chemotherapeutic agents) in combination with an inhibitor specific for the p42/44 mitogen-activated protein (MAP) kinase cascade "proper". Inhibition of the p42/44 MAP kinase cascade with an agent such as PD184352 inhibits the ability of Raf protein kinases to phosphorylate and activate the enzymes MEK1 and MEK2. This in turn potentiates the apoptotic activity of radiation and the chemotherapeutic agents ara-C and taxol.

IT 305350-87-2, SL 327
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes tumor cells)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



No with good date NO 102(a)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

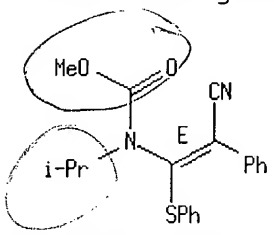
ACCESSION NUMBER: 1985:113373 HCAPLUS
DOCUMENT NUMBER: 102:113373
TITLE: C-(Methoxycarbonyl)ketene N-imidoylimine synthesis and rearrangement into methyl 4,6-diazahepta-2,4,6-trienoates. Cycloaddition reactions with isocyanides: preparation of imidazolines
AUTHOR(S): Morel, Georges; Marchand, Evelyne; Foucaud, Andre
CORPORATE SOURCE: Groupe Chim. Struct., Univ. Rennes, Rennes, 35042, Fr.
SOURCE: Journal of Organic Chemistry (1985), 50(6), 771-8
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:113373

AB Ketene N-imidoylimines were shown to be transitory intermediates formed by the reaction of isocyanides with (alkylthio)cyanoacetate esters or by the reaction of imino chloro sulfides with Na salts of α-cyano esters. When the N atom of the imidoyl group bore a primary or secondary substituent, the ketene imines were converted into diazatrienes by a very fast 1,5-migration of the H atom of the imidoyl group. Certain

diazatrienes bearing a cyano group underwent an intramol. [4 + 2] cycloaddn. to form dihydropyrrolotriazines. The diazatrienes could be trapped by a regiospecific [1 + 4] cycloaddn. with isocyanides to give imidazolines.

IT **94518-73-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 94518-73-7 HCAPLUS
CN Carbamic acid, [2-cyano-2-phenyl-1-(phenylthio)ethenyl](1-methylethyl)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

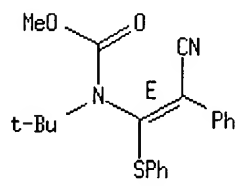
Full Text | Citing References

ACCESSION NUMBER: 1984:406766 HCAPLUS
DOCUMENT NUMBER: 101:6766
TITLE: Synthesis of thioimidates by insertion of tert-butyl isocyanide into the carbon-sulfur bond of activated sulfides. Rearrangement of thioimidates by 1,3 carbon-to-nitrogen migration of an alkoxycarbonyl group
AUTHOR(S): Morel, G.; Marchand, E.; Thi, K. H. Nguyen; Foucaud, A.
CORPORATE SOURCE: Groupe Chim. Struct., Univ. Rennes, Rennes, 35042, Fr.
SOURCE: Tetrahedron (1984), 40(6), 1075-83
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 101:6766

AB Me3CNC inserts into the carbon-sulfur bond of RR1C(CN)SR2 (R = MeO2C, EtO2C; R1 = PhCH2, aryl, H, etc.; R2 = Me, Ph, PhCH2) to give thioimidates RR1C(CN)C(SR2):NCMe3. The thioimidates can also be obtained via the chlorine substitution of Me3CN:CClSR2, which is a more general method. These thioimidates rearrange to E and Z isomers of N-vinylcarbamates via a 1,3 C to N migration of the alkoxycarbonyl group.

IT **90496-37-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 90496-37-0 HCAPLUS
CN Carbamic acid, [2-cyano-2-phenyl-1-(phenylthio)ethenyl](1,1-dimethylethyl)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

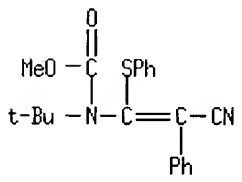
Full Text | Citing References

ACCESSION NUMBER: 1982:527210 HCAPLUS
DOCUMENT NUMBER: 97:127210
TITLE: Uncatalyzed insertion reaction of isocyanides into a carbon-sulfur bond
AUTHOR(S): Morel, G.; Marchand, E.; Nguyen Thi, K. H.; Foucaud, A.
CORPORATE SOURCE: Groupe Physiochim. Struct., Univ. Rennes, Rennes, 35042, Fr.
SOURCE: Tetrahedron Letters (1982), 23(19), 2023-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 97:127210

AB RNC (I; R = Me3C, tert-octyl) with R1C(CN)(SR2)CO2Me [II; R1 = Ph2C(CN), R2 = Me, Ph, PhCH2; R1 = 5-cyanofluoren-5-yl, (PhCH2)2C(CN), PhCMe(CN), PhCEt(CN), R2 = Me] at room temp. for 17-114 h gave 36-84% RN:C(SR2)CR1(CN)CO2Me (III). III (R2 ≠ Ph) are unstable and rearrange at room temp. to give E- and Z-RN(CO2Me)C(SR2):CR1(CN) (E- and Z-IV) in 6-82% yield. I with II [R1 = p-R3C6H4 (R3 = Cl, Me, MeO, NO2), PhCH2, R2 = Me; R1 = p-MeC6H4, R2 = PhCH2; R1 = R2 = Ph] in reluxing MeCN gave the corresponding E- and Z-IV in 19-94% yield.

IT **82940-24-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 82940-24-7 HCAPLUS
CN Carbamic acid, [2-cyano-2-phenyl-1-(phenylthio)ethenyl](1,1-dimethylethyl)-, methyl ester (9CI) (CA INDEX NAME)



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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.32	-8.32

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent

assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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L1             STRUCTURE UPLOADED
L2              4 S L1
L3             84 S L1 FULL

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L5              1 S L4 AND HOBBS, F?/AU
L6             11 S L4 NOT L5

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L7              0 L3

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NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
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NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN
NEWS 21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
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NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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DICTIONARY FILE UPDATES:    6 JUN 2004  HIGHEST RN 690209-28-0

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L1       STRUCTURE UPLOADED

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L1               STR

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SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO       504
PROJECTED ANSWERS:               4 TO       200

L2             4 SEA SSS SAM L1

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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SEARCH TIME: 00.00.01

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COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                              155.42     155.63
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FILE COVERS 1907 - 7 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 6 Jun 2004 (20040606/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L9           2 L4 AND TUM?

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L9   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

ACCESSION NUMBER: 2002:256049 HCAPLUS
DOCUMENT NUMBER: 136:257237
TITLE: **Tumor** cell killing by cell cycle checkpoint abrogation combined with inhibition of the "classical" mitogen activated protein (MAP) kinase pathway

INVENTOR(S): Dent, Paul; Grant, Steven; McKinstry, Robert; Dai, Yum
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026236	A1	20020404	WO 2001-US30508	20010928
WO 2002026236	C2	20030220		

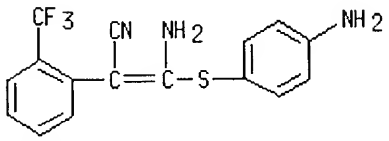
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-235938P P 20000928

AB The present invention provides a method for treating cancer by promoting apoptosis and reducing clonogenic survival of cancer cells. The method encompasses co-administering 1) a cell cycle checkpoint abrogation agent (for example, UCN-01 or caffeine) and 2) an inhibitor of a compensatory cytoprotective pathway, such as an agent that inhibits the MEK 1/2 pathway (e.g.; PD98059, U0126, or PD184352) or an agent that inhibits the PI 3 pathway (e.g.; LY294002 or wortmanin). In addn., because the co-administration step also radiosensitizes cancer cells, the method addnl. encompasses the administration of radiation to further reduce clonogenic survival of cancer cells. The method promotes apoptosis and reduces clonogenic survival in many types of cancer cells, including leukemia cells, prostate cancer cells, breast cancer cells, myeloma cells, and lymphoma cells.

IT **305350-87-2**, SL 327
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**tumor** cell killing by cell cycle checkpoint abrogation combined with inhibition of MAP kinase pathway)

RN 305350-87-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:805039 HCAPLUS
DOCUMENT NUMBER: 133:344610
TITLE: Specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes **tumor** cells

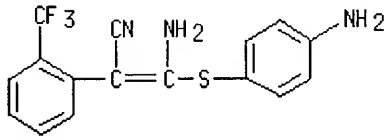
INVENTOR(S): Dent, Paul; Grant, Steven; Jarvis, W. David
PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
SOURCE: U.S., 19 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6147107	A	20001114	US 1998-203342	19981220

PRIORITY APPLN. INFO.: US 1998-203342 19981220

AB Mammalian cancer cells are effectively killed when treated with a lethal agent (e.g. radiation or chemotherapeutic agents) in combination with an inhibitor specific for the p42/44 mitogen-activated protein (MAP) kinase cascade "proper". Inhibition of the p42/44 MAP kinase cascade with an agent such as PD184352 inhibits the ability of Raf protein kinases to phosphorylate and activate the enzymes MEK1 and MEK2. This in turn potentiates the apoptotic activity of radiation and the chemotherapeutic agents ara-C and taxol.

IT 305350-87-2, SL 327
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(specific inhibition of the p42/44 mitogen-activated protein kinase cascade sensitizes **tumor** cells)
RN 305350-87-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 08:16:48 ON 07 JUN 2004
L1 STRUCTURE UPLOADED
L2 4 S L1
L3 84 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 08:17:30 ON 07 JUN 2004
L4 7 S L3/THU
L5 0 S L4 AND ARTHRIT?
L6 0 S L4 AND PERIODON?
L7 0 S L4 AND GINGIV?
L8 0 S L4 AND ULCER?
L9 2 S L4 AND TUM?

=> s l4 and neovasc?
5197 NEOVASC?
L10 0 L4 AND NEOVASC?

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         17307 GLAUC?
L11           0 L4 AND GLAUC?

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         31709 SCLER?
L12           0 L4 AND SCLER?

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         10273 PSORIAS?
L13           0 L4 AND PSORIAS?

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L14           0 L4 AND CARDIO?

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         29755 HEMORR?
L15           0 L4 AND HEMORR?

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L16           0 L4 AND COAG?

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          4387 CACH?
L17           0 L4 AND CACH?

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          7699 ANORE?
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        536032 ALC
        178589 ALCS
        627344 ALC
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        761326 ALCOHO?
                 (ALCOHO? OR ALC)
L19           0 L4 AND ALCOHO?

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        129362 SHOC?
L21           0 L4 AND SHOC?

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L22           0 L4 AND GRAFT?

=> s l4 and auto?
        582677 AUTO?
L23           0 L4 AND AUTO?

=> s l4 and infec?
        324768 INFEC?
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L24           0 L4 AND INFEC?

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     FILE 'REGISTRY' ENTERED AT 08:16:48 ON 07 JUN 2004
L1               STRUCTURE UPLOADED
L2             4 S L1
L3            84 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 08:17:30 ON 07 JUN 2004
L4             7 S L3/THU
L5             0 S L4 AND ARTHRIT?
L6             0 S L4 AND PERIODON?
L7             0 S L4 AND GINGIV?
L8             0 S L4 AND ULCER?
L9             2 S L4 AND TUM?
L10            0 S L4 AND NEOVASC?
L11            0 S L4 AND GLAUC?
L12            0 S L4 AND SCLER?
L13            0 S L4 AND PSORIAS?
L14            0 S L4 AND CARDIO?
L15            0 S L4 AND HEMORR?
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L21            0 S L4 AND SHOC?
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L23            0 S L4 AND AUTO?
L24            0 S L4 AND INFEC?

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L25            5 L4 NOT L9

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L25  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:          2003:153388  HCAPLUS
DOCUMENT NUMBER:           138:198569
TITLE:                     Use of kinase-inhibiting agents for prophylaxis and/or
                           therapy of viral diseases, and system for
                           identification of such agents
INVENTOR(S):               Ludwig, Stephan; Planz, Oliver; Sedlacek, Hans-Harald;
                           Pleschka, Stephan
PATENT ASSIGNEE(S):        Medinnova Gesellschaft fur Medizinische Innovationen
                           aus Akademischer Forschung m.b.H., Germany
SOURCE:                    Ger. Offen., 10 pp.
                           CODEN: GWXXBX
DOCUMENT TYPE:             Patent
LANGUAGE:                  German
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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DE 10138912 A1 20030227 DE 2001-10138912 20010808
WO 2003015689 A2 20030227 WO 2002-DE2810 20020726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

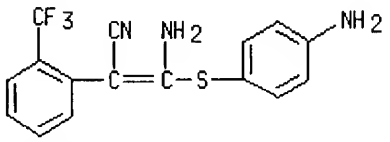
PRIORITY APPLN. INFO.: DE 2001-10138912 A 20010808

AB The invention discloses the use of at least one, preferably two, active substance(s) for the prophylaxis and/or therapy of at least one viral disease, characterized in that the active substance(s) inhibit either a signal transduction pathway-assocd. kinase such that virus replication is essentially inhibited or a SEK kinase.

IT **305350-87-2**, SL 327
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(kinase-inhibiting agents for prophylaxis and/or therapy of viral diseases, and system for identification of such agents)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:12017 HCAPLUS
DOCUMENT NUMBER: 138:396146
TITLE: Significant neuroprotection against ischemic brain injury by inhibition of the MEK1 protein kinase in mice: Exploration of potential mechanism associated with apoptosis
AUTHOR(S): Wang, Xinkang; Wang, Hugh; Xu, Lin; Rozanski, Dennis J.; Sugawara, Taku; Chan, Pak H.; Trzaskos, James M.; Feuerstein, Giora Z.
CORPORATE SOURCE: Department of Cardiovascular Sciences, Bristol-Myers Squibb Company, Wilmington, DE, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2003), 304(1), 172-178
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

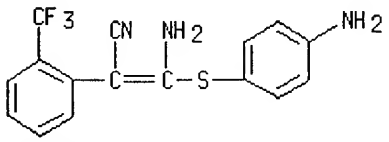
AB MEK1/2 is a serine/threonine protein kinase that phosphorylates and activates extracellular signal-responsive kinase (ERK)1/2. In the present study we explored the role of MEK1/2 in ischemic brain injury using a

selective MEK1/2 inhibitor, SL327, in mice. C57BL/6 mice were subjected to a 30-min occlusion of the middle cerebral artery (MCAO) followed by reperfusion. Western blot anal. demonstrated the immediate activation of MEK/ERK after reperfusion (within the first 10 min) in the ischemic brain; this activation was dose dependently blocked by SL327 (10-100 mg/kg, i.p.). A single dose of SL327 (100 mg/kg) administered 15 min before or 25 min after the onset of ischemia resulted in 63.6% ($n = 18$, $p < 0.001$) and 50.7% ($n = 18$, $p < 0.01$) redn. in infarct size, resp., compared with vehicle-treated mice. Similarly, SL327 significantly reduced neurol. deficits 1 to 3 days after reperfusion ($n = 12$, $p < 0.01$). The salutary effect of SL327-induced neuroprotection was independent of mitochondrial cytochrome c release or caspase-8-mediated apoptosis; however, SL327 markedly suppressed the levels of active caspase-3 and DNA fragmentation (as a measure of apoptosis) after ischemia/reperfusion. Our data suggest that the inhibition of MEK1/2 results in neuroprotection from reperfusion injury and that this protection may be assocd. with the redn. in apoptosis.

IT 305350-87-2, SL 327
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(apoptosis-assocd. mechanism of neuroprotection against ischemic brain damage by inhibition of MEK1 protein kinase)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:574917 HCAPLUS
DOCUMENT NUMBER: 137:135102
TITLE: Inhibition of extracellular signal-regulated kinases (ERKs) reduces or prevents both tolerance to and dependence on opioid analgesics and sensitization after painful stimulation
INVENTOR(S): Gutstein, Howard B.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058687	A2	20020801	WO 2002-US2128	20020125
WO 2002058687	A3	20031009		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1377279 A2 20040107 EP 2002-717370 20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

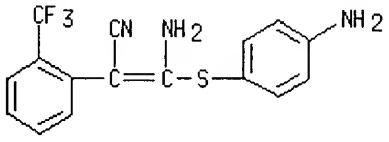
PRIORITY APPLN. INFO.: US 2001-264336P P 20010125
WO 2002-US2128 W 20020125

AB Inhibition of mitogen-activated protein kinases (MAPKs), or more particularly extracellular signal-regulated kinases (ERKs) inhibits the development of tolerance to opioid analgesics. Therefore, methods for reducing tolerance, reducing the risk of phys. dependence, reducing hyperalgesia, reducing the symptoms of opioid withdrawal or inhibiting pain sensitization are described. MAPK inhibition at the spinal level represents a powerful treatment modality for chronic pain, blocking both neural sensitization induced by pain and factors limiting the effectiveness of opioids, the strongest analgesics currently in use to treat chronic pain.

IT 305350-87-2, SL 327
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibition of extracellular signal-regulated kinases reduces or prevents tolerance to and dependence on opioid analgesics)

RN 305350-87-2 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L25 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:31238 HCAPLUS
DOCUMENT NUMBER: 136:79789
TITLE: Methods for treating seizure disorders by inhibiting MAPK pathway activation
INVENTOR(S): Sweatt, J. David; Anderson, Anne E.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002097	A2	20020110	WO 2001-US20773	20010629
WO 2002002097	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

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UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

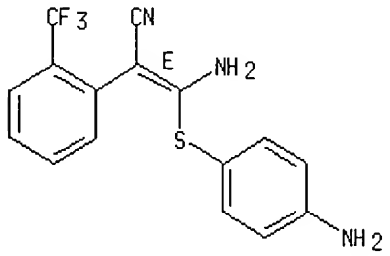
US 2002058699 A1 20020516 US 2001-893754 20010629
PRIORITY APPLN. INFO.: US 2000-215221P P 20000630
OTHER SOURCE(S): MARPAT 136:79789

AB Excessive brain neuronal excitability, assocd. with a seizure disorder, can be correlated with increased mitogen-activated protein kinase (MAPK) activity in neurons. Such excessive excitability can be ameliorated by administering an effective amt. of a compd., such as a MAPK phosphorylation or kinase activity inhibitor, that reduces the amt. of MAPK activity in neurons of an individual suffering from a seizure disorder. Compds. that inhibit phosphorylation or kinase activity of upstream activators or downstream targets of the MARPK cascade also are useful in this context.

IT **297744-40-2P**, (E)-SL 327
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(anticonvulsant treatment with inhibitors of mitogen-activated protein kinase pathway activation)

RN 297744-40-2 HCAPLUS
CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)-, (αE)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L25 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:688212 HCAPLUS
DOCUMENT NUMBER: 133:266611
TITLE: Preparation of amino-thio-acrylonitriles as MEK inhibitors
INVENTOR(S): Hobbs, Frank W.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000056706	A1	20000928	WO 2000-US7262	20000315

W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ,

PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

EP 1163215 A1 20011219 EP 2000-916525 20000315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

US 6703420 B1 20040309 US 2000-527335 20000317
US 2004087583 A1 20040506 US 2003-697531 20031030

PRIORITY APPLN. INFO.: US 1999-125330P P 19990319
WO 2000-US7262 W 20000315
US 2000-527335 A3 20000317

OTHER SOURCE(S): CASREACT 133:266611; MARPAT 133:266611

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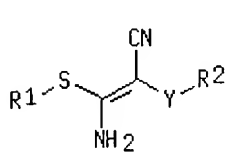

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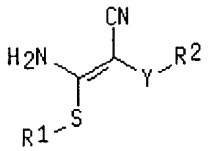


II

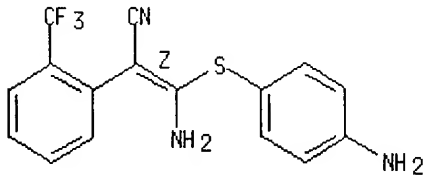
AB The title compds. [I or II; R1 = (un)substituted Ph, naphthyl, 2,3-dihydroindol-5-yl, etc.; Y = (un)substituted Ph, naphthyl, CHR3; R2 = H, (un)substituted Ph, naphthyl, etc.; R3 = (un)substituted Ph, naphthyl], MEK inhibitors useful for treatment and prevention of inflammatory disorders or as an anticancer radiosensitizing agents, were prepd. and formulated. E.g., a 2-step synthesis of I and II [R1 = 4-H2NC6H4; YR2 = 2-F3CC6H4], starting with 2-trifluoromethyl-1-iodobenzene and malononitrile, was given. Compds. I and II are effective at 1.0-20 mg/kg/day (oral administration).

IT **297744-39-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino-thio-acrylonitriles as MEK inhibitors)

RN 297744-39-9 HCAPLUS

CN Benzeneacetonitrile, α-[amino[(4-aminophenyl)thio]methylene]-2-(trifluoromethyl)-, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 08:16:48 ON 07 JUN 2004
L1 STRUCTURE UPLOADED
L2 4 S L1

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L3            84 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 08:17:30 ON 07 JUN 2004
L4             7 S L3/THU
L5             0 S L4 AND ARTHRIT?
L6             0 S L4 AND PERIODON?
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L10            0 S L4 AND NEOVASC?
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L16            0 S L4 AND COAG?
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L20            0 S L4 AND ACUTE?
L21            0 S L4 AND SHOC?
L22            0 S L4 AND GRAFT?
L23            0 S L4 AND AUTO?
L24            0 S L4 AND INFEC?
L25            5 S L4 NOT L9

=> s l3
L26           12 L3

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FULL ESTIMATED COST                                    49.81     205.44

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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FILE LAST UPDATED:  01 May 1997 (19970501/UP)

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  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

  This file supports REG1stRY for direct browsing and searching of
  all substance data from the REGISTRY file.  Enter HELP FIRST for
  more information.

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     FILE 'REGISTRY' ENTERED AT 08:16:48 ON 07 JUN 2004
L1                STRUCTURE UPLOADED
L2              4 S L1
L3             84 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 08:17:30 ON 07 JUN 2004
L4              7 S L3/THU
L5              0 S L4 AND ARTHRIT?
L6              0 S L4 AND PERIODON?
L7              0 S L4 AND GINGIV?
L8              0 S L4 AND ULCER?
L9              2 S L4 AND TUM?
L10             0 S L4 AND NEOVASC?
L11             0 S L4 AND GLAUC?
L12             0 S L4 AND SCLER?
L13             0 S L4 AND PSORIAS?
L14             0 S L4 AND CARDIO?
L15             0 S L4 AND HEMORR?
L16             0 S L4 AND COAG?
L17             0 S L4 AND CACH?
L18             0 S L4 AND ANORE?
L19             0 S L4 AND ALCOHO?
L20             0 S L4 AND ACUTE?
L21             0 S L4 AND SHOC?
L22             0 S L4 AND GRAFT?
L23             0 S L4 AND AUTO?
L24             0 S L4 AND INFEC?
L25             5 S L4 NOT L9
L26            12 S L3

     FILE 'CAOLD' ENTERED AT 08:21:27 ON 07 JUN 2004

=> s l3
L27             0 L3

=>
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* * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20	May 17	FRFULL now available on STN
NEWS 21	May 27	STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS 22	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 23	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 24	May 27	Explore APOLLIT with free connect time in June 2004

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:31:38 ON 07 JUN 2004

=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:32:13 ON 07 JUN 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JUN 2004 HIGHEST RN 690209-28-0
DICTIONARY FILE UPDATES: 6 JUN 2004 HIGHEST RN 690209-28-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> **file hcaplus**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.63

FILE 'HCAPLUS' ENTERED AT 11:32:18 ON 07 JUN 2004
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FILE COVERS 1907 - 7 Jun 2004 VOL 140 ISS 24
FILE LAST UPDATED: 6 Jun 2004 (20040606/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> **s mek () kinase and rheumatoid ?arthri?**
16247 MEK
97 MEKS
16278 MEK
(MEK OR MEKS)
216547 KINASE
43412 KINASES
223780 KINASE

```
                (KINASE OR KINASES)
          855 MEK (W) KINASE
        22652 RHEUMATOID
           11 RHEUMATOIDS
        22656 RHEUMATOID
                (RHEUMATOID OR RHEUMATOIDS)
        41347 ?ARTHRI?
        19616 RHEUMATOID ?ARTHRI?
                (RHEUMATOID(W)?ARTHRI?)
L1          8 MEK (W) KINASE AND RHEUMATOID ?ARTHRI?

=> s l1 and review/dt
      1732111 REVIEW/DT
L2          0 L1 AND REVIEW/DT

=> s MEK () kinase and ?arthri?
        16247 MEK
           97 MEKS
        16278 MEK
                (MEK OR MEKS)
       216547 KINASE
        43412 KINASES
       223780 KINASE
                (KINASE OR KINASES)
          855 MEK (W) KINASE
        41347 ?ARTHRI?
L3         19 MEK (W) KINASE AND ?ARTHRI?

=> s l3 and review/dt
      1732111 REVIEW/DT
L4          1 L3 AND REVIEW/DT

=> d l4, ibib abs, 1

L4   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
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Full Text | Citing References

```
ACCESSION NUMBER:         2003:41831  HCAPLUS
DOCUMENT NUMBER:          139:177
TITLE:                    Developments in mitogen-induced extracellular kinase 1
                          inhibitors and their use in the treatment of disease
AUTHOR(S):                Krepinsky, Joan; Wu, Dongcheng; Ingram, Alistair;
                          Scholey, James; Tang, Damu
CORPORATE SOURCE:         Department of Medicine, University of Toronto,
                          Toronto, ON, Can.
SOURCE:                   Expert Opinion on Therapeutic Patents (2002), 12(12),
                          1795-1811
                          CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER:                Ashley Publications Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  Multiple signal transduction pathways converge on the
     Raf-mitogen-induced extracellular kinase (MEK)-extracellular
     signal-regulated kinase (Erk) cascade to effect diverse cellular
     processes, including proliferation, differentiation, survival, apoptosis
     and organ functions such as memory consolidation.  Improper activation of
     this pathway contributes significantly to numerous diseases, including
     cancer and various immune disorders.  Specific inhibition of this
     signaling cascade thus offers great therapeutic potential for many
     diseases.  Since the discovery of the first MEK1 inhibitor in 1995,
```

several novel classes of inhibitors, with varying selectivity for MEK1, have been developed. Clin. applications for some of these have been investigated, with the majority focusing on proliferative diseases in which abnormally increased Erk activity plays a major role, most notably cancer, or immunol. and inflammatory conditions such as **arthritis** and organ transplant rejection. To a lesser extent, ischemia/reperfusion (I/R) injury and chronic pain disorders have also been targeted.

REFERENCE COUNT: 142 THERE ARE 142 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s MEK () kinase and periodont?
         16247 MEK
            97 MEKS
         16278 MEK
                  (MEK OR MEKS)
        216547 KINASE
         43412 KINASES
        223780 KINASE
                  (KINASE OR KINASES)
           855 MEK (W) KINASE
          8974 PERIODONT?
L5           0 MEK (W) KINASE AND PERIODONT?

=> s MEK () kinase and ?odont?
         16247 MEK
            97 MEKS
         16278 MEK
                  (MEK OR MEKS)
        216547 KINASE
         43412 KINASES
        223780 KINASE
                  (KINASE OR KINASES)
           855 MEK (W) KINASE
         15323 ?ODONT?
L6           0 MEK (W) KINASE AND ?ODONT?

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            97 MEKS
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                  (MEK OR MEKS)
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        223780 KINASE
                  (KINASE OR KINASES)
           855 MEK (W) KINASE
         11961 GING?
L7           0 MEK (W) KINASE AND GING?

=> s MEK and ging?
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         16278 MEK
                  (MEK OR MEKS)
         11961 GING?
L8           4 MEK AND GING?

=> s l8 and review/dt
```

```
       1732111 REVIEW/DT
L9           0 L8 AND REVIEW/DT

=> s MEK () kinase and ulcer?
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         43412 KINASES
        223780 KINASE
                 (KINASE OR KINASES)
           855 MEK (W) KINASE
         32441 ULCER?
L10          3 MEK (W) KINASE AND ULCER?

=> s l10 and review/dt
       1732111 REVIEW/DT
L11          0 L10 AND REVIEW/DT

=> d l10, ibib abs fhitstr, 1-5

L10  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
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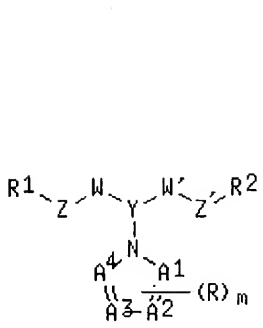
Full Text | Citing References

ACCESSION NUMBER: 2003:335087 HCAPLUS
DOCUMENT NUMBER: 138:353989
TITLE: Preparation of N-(imidazolylmethyl)benzamides and imidazolylalkyl-benzoates as MEK-1 and ERK-2 kinase inhibitors
INVENTOR(S): Arkinstall, Stephen J.; Arulanandam, Antonio; Jiang, Xuliang; Magar, Sharad; Nabioullin, Roustem; Zhang, John Yingsheng; Blume-Jensen, Peter
PATENT ASSIGNEE(S): Applied Research Systems ARS Holding N.V., Neth. Antilles
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035626	A2	20030501	WO 2002-US33963	20021023
WO 2003035626	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-336040P P 20011023
OTHER SOURCE(S): MARPAT 138:353989
GI



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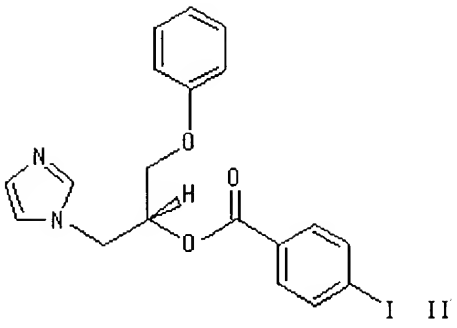

I II

AB Title compds. I [A1-4 = C, N with at least one A1-4 = C; R = halo, NO2, (hetero)alk(en/yn)yl, etc.; m = integer; Y = (hetero)alk(en/yn)yl; W, W' = hetero atom, heteroalkyl, etc.; Z, Z' = bond, alkanoyl; R1-2 = (un)substituted carbocyclic aryl, heteroarom.] are prepd. For instance, (S)-glycidol was treated with phenol (THF, PPh3,DEAD) and the product treated with imidazole and finally coupled with p-iodobenzoic acid to give II. II had IC50 = 39 nM for MEK-1 kinase and 36 nM in the MEK-1/ERK-2 kinase assay. I are useful for a variety of therapies, including treating or preventing various cancers, inflammation, septic shock, preterm labor, infertility, pain, ischemia and other diseases and disorders assocd. with MEK-1 and/or ERK-2 activation.

L10 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:920949 HCAPLUS
DOCUMENT NUMBER: 136:384702
TITLE: Interleukin-1β induces cyclo-oxygenase-2 expression in gastric cancer cells by the p38 and p44/42 mitogen-activated protein kinase signaling pathways
AUTHOR(S): Fan, Xiao Ming; Wong, Benjamin Chun Yu; Lin, Marie Chia Mi; Cho, Chi Hin; Wang, Wei Ping; Kung, Hsiang Fu; Lam, Shiu Kum
CORPORATE SOURCE: Department Of Medicine, University of Hong Kong, Hong Kong, Hong Kong
SOURCE: Journal of Gastroenterology and Hepatology (2001), 16(10), 1098-1104
CODEN: JGHEEO; ISSN: 0815-9319
PUBLISHER: Blackwell Science Asia Pty Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyclo-oxygenase-2 (COX-2) is the inducible enzyme in the gastric mucosa responsible for prostaglandin prodn. during inflammation and **ulcer** healing. The regulation of COX-2 gene expression in gastric epithelial cells is not well understood. Here, the authors investigated the effect of interleukin (IL)-1β on COX-2 expression in the human gastric cancer cell, and explored the signaling pathways involved. Gastric cancer cell line AGS was treated with IL-1β or the inhibitors of mitogen-activated protein-Erk kinase (MEK) and p38 mitogen-activated protein (MAP) kinase prior to the addn. of IL-1β. The COX-2 mRNA or protein levels were measured by using RT-PCR or western blot anal., resp. Prostaglandin E2 (PGE2) prodn./secretion was detd. by using the PGE2 EIA assay. The phosphorylation/activation of p44/42 and p38 MAP kinases were detd. by using western blot anal. and using phospho-specific antibodies.

Interleukin-1β treatment dose- and time-dependently increased COX-2 mRNA and protein expression levels, and enhanced PGE2 prodn./secretion in AGS cells. In contrast, IL-1β had no effect on the level of the constitutively expressed COX-1. In parallel to the increase of COX-2, the authors showed that p44/42 and p38 MAP kinase activities were also upregulated by IL-1β treatment. To demonstrate the cause-effect relation, the authors showed that inhibition of MEK and p38 MAP kinase with specific inhibitors suppressed IL-1β-mediated increases in COX-2 mRNA and protein levels, and the PGE2 prodn. Thus, in human gastric cancer cells, IL-1β upregulates the COX-2 gene expression via the activation of MEK/p44/42 and p38 MAP kinases pathway.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:826627 HCAPLUS
DOCUMENT NUMBER: 136:323877
TITLE: Expression of cyclooxygenase-2 in human neutrophils activated by Helicobacter pylori water-soluble proteins: Possible involvement of NF-κB and MAP kinase signaling pathway
AUTHOR(S): Kim, Joo Sung; Kim, Jung Mogg; Jung, Hyun Chae; Song, In Sung
CORPORATE SOURCE: Department of Internal Medicine, Seoul National University College of Medicine, Seoul, 110-744, S. Korea
SOURCE: Digestive Diseases and Sciences (2001), 46(10), 2277-2284
CODEN: DDSCDJ; ISSN: 0163-2116
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB H. pylori infection elicits persistent neutrophil infiltration in gastric mucosa. The expression of cyclooxygenase (COX)-2 by the neutrophils results in prostaglandin (PG) E2 synthesis, which may account for alterations in tissue homeostasis. Here, the authors found that COX-2 mRNA was up-regulated in the neutrophils when stimulated with both H. pylori water ext. (HPWE) and live H. pylori in a transwell model and detd. by quant. RT-PCR. PGE2 synthesis was also enhanced in the neutrophils activated by both the HPWE and live H. pylori. A specific COX-2 inhibitor (NS-398) blocked PGE2 synthesis, and an anti-**ulcer** agent (rebamipide) suppressed it dose dependently. An NF-κB inhibitor (pyrrolidine dithiocarbamate), a MAP kinase (MEK) inhibitor (PD98059), and a p38 MAP kinase inhibitor (SB203580) suppressed the COX-2 gene transcription and PGE2 synthesis in the neutrophils. Thus, H. pylori water-sol. proteins may enhance the COX-2 expression, and this action could be mediated through the NF-κB and MAP kinase signaling pathways. The increased secretion of PGE2 by the neutrophils may play a proinflammatory role in the gastric mucosal response to H. pylori.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	29.04	29.67

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.77	-2.77

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